

## **EFFECT OF SODIUM VALPROATE ON GROWTH, CARCASS QUALITY, SERUM PROTEIN AND CHOLESTEROL IN RABBITS**

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Growth of rabbits for broiler purpose could be achieved by scrupulous managerial practices such as improved feeding (feed efficiency) or reduction of feed wastage. This can be further improved through pharmacological manipulation by drugs at far low doses than that are being used for therapeutic purposes. The pharmacological agents initiate a series of biological events which include involvement of neurotransmitter system like GABAergic, serotonergic, histaminergic etc. towards growth promotion.

A variety of substances including benzodiazepines have been examined for their potential as appetite stimulants. Benzodiazepine group of compounds are considered to increase feed intake by increasing GABA concentrations in the brain in ruminants (Baile and McLaughlin, 1987) and in rats (Poschel, 1971). Sodium valproate (SV) - a putative GABA agonist which induced increase in body weight in man have been associated with an increase in fatty tissue due to an elevated appetite (Dinesen *et al.*, 1984 and Dulac *et al.*, 1986).

The present study was undertaken to investigate the effect of Sodium valproate (SV) on feed intake, body weight gain, feed efficiency, carcass quality, serum total protein and cholesterol in rabbits.

### **Materials and Methods**

Healthy weaned 40 days old New Zealand White cross-bred male rabbits, weighing over 400 g were selected. The rabbits were trained for five days with ad libitum feed and water to get them acclimatized before starting the experiment. The rabbits were housed in individual wire-mesh cages (18" x 18" x 24") in a well ventilated room. Individual feeding cups and water bottles were provided in the cages for daily feeding and watering.

Rabbits were randomly allotted to four groups, each group comprising of six animals. The average body weight between groups did not differ more than twelve grams. The concentrate feed and green fodder for rabbits supplied by the Livestock

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Research Station, Kattupakkam were used during the study. The ration was computed as per the NRC requirements of rabbits fed *ad libitum* (energy - 2500 Kcal and crude protein - 16%). The concentrate feed and fodder were analysed for proximate composition and offered to rabbits as per NRC requirements.

The rabbits were offered pre-weighed quantities of concentrate feed and green fodder (*Desmanthus virgatus*) for 24 hours from seventh to sixteenth week of age (10 weeks). The left-over concentrate feed and green fodder were weighed daily to calculate the cumulative feed intake. Daily samples of concentrate feed, green fodder and left over were analysed for moisture content in order to calculate the cumulative feed intake on dry matter basis.

Sodium valproate (SV) dissolved in normal saline was administered orally at the rate of one ml per animal. The drug was administered daily between 8.30 and 9.00 a.m. using a mouth gag and an eustachian tube with the rabbit secured on its back. Normal saline was administered at the rate of one ml per animal in the control group. SV in normal saline was administered to the animals of three treatment groups at the rate of 10, 15 and 20 mg/kg per day from seventh week to the end of sixteenth week of age.

Individual feed intake and body weight were recorded daily from sixth to sixteenth week to calculate weekly cumulative feed intake, weight gain and feed efficiency.

The animals were slaughtered at the end of sixteen weeks of age, 24 hours after the administration of last dose of the drug as

described by Romans and Ziegler (1974). The carcass weight and dressing percentage were determined. The loin eye area of the muscle (longissimus muscle) was measured to find out the lean meat content of the carcass. The carcass composition viz. carcass protein and carcass fat of meat collected from thigh and longissimus muscle, was estimated (Holmes *et al.*, 1984).

At the end of the experiment, blood samples were collected from the ear vein and serum samples were used for the estimation of total proteins (Dumas *et al.*, 1981) and serum cholesterol (Wybenga *et al.*, 1970). The data were analysed by unpaired 't' test (Snedecor and Cochran, 1967).

## Results and Discussion

The effect of oral administration of 10, 15 and 20 mg/kg of sodium valproate (SV) - a putative GABA agonist, on feed intake, weight gain, feed efficiency, carcass quality and biochemical changes was studied in rabbits. The duration of the study was ten weeks i.e. from seventh to sixteenth week of age.

The cumulative feed intake of SV treated groups showed highly significant ( $P < 0.01$ ) increase in feed intake in all the three doses consistently, throughout the period (Table 1). SV at 10 and 15 mg/kg caused highly significant ( $P < 0.01$ ) increase in the body weight from eight to sixteen weeks whereas 20 mg/kg dose level produced a similar increase from seventh week itself (Table 2).

All the three doses showed significant ( $P < 0.05$ ) improvement in feed efficiency (Table 3). Shephard and Estall (1984)

Table 1 Effect of sodium valproate on cumulative feed intake in rabbits (Mean<sup>#</sup> ± SEM)

Period	Cumulative feed intake (g)			
	Control	SV 10mg/kg	SV 15mg/kg	SV 20mg/kg
6th week*	220±5.14	218±4.64	220±3.40	217±4.87
7th week	320±5.58	357±1.58**	433±1.15**	446±8.86**
8th week	673±9.50	738±2.79**	879±2.69	898±10.60**
9th week	1047±10.87	1141±5.57**	1335±5.57**	1364±15.66**
10th week	1431±11.95	1578±10.68**	1802±7.01**	1840±21.21**
11th week	1832±12.90	2038±13.25**	2273±12.76**	2348±22.39**
12th week	2251±16.03	2530±11.71**	2774±13.93**	2852±26.33**
13th week	2689±18.85	3048±11.29**	3287±17.84**	3370±28.29**
14th week	3165±22.18	3573±10.65**	3808±21.85**	3908±33.72**
15th week	3644±22.31	4095±16.13**	4366±22.90**	4474±35.88**
16th week	4131±22.76	4613±19.77**	4938±24.59**	5053±36.69**

<sup>#</sup> Mean values are based upon 6 number of observations

\* Without drug and saline treatment

\*\* Highly significant (P<0.01)

Table 2 Effect of sodium valproate on cumulative weight gain in rabbits (Mean<sup>#</sup> ± SEM)

Period	Cumulative weight gain (g)			
	Control	SV 10 mg/kg	SV 15 mg/kg	SV 20 mg/kg
6th week*	32±1.05	32±1.05	31±1.83	31±0.83
7th week	70±2.24	76±0.83	75±1.83	98±4.77**
8th week	159±6.11	192±4.01**	203±1.67**	243±7.38**
9th week	254±13.93	326±6.51**	348±1.12**	398±8.43**
10th week	370±14.72	471±7.35**	499±2.01**	557±9.28**
11th week	499±14.91	623±7.27**	653±2.47**	717±10.39**
12th week	625±11.97	778±6.54**	814±3.33**	878±10.78**
13th week	757±10.78	936±7.35**	971±3.52**	1048±10.38**
14th week	882±10.78	1075±7.07**	1126±3.52**	1215±12.58**
15th week	997±9.28	1201±7.00**	1282±4.41**	1378±15.32**
16th week	1107±6.54	1321±7.57**	1438±3.82**	1538±18.01**

<sup>#</sup> Mean values are based upon 6 number of observations

\* Without drug and saline treatment

\*\* Highly significant (P<0.01)

Table 3 Effect of sodium valproate on cumulative feed efficiency in rabbits (Mean<sup>#</sup>±SEM)

Period	Cumulative feed efficiency			
	Control	SV 10 mg/kg	SV 15 mg/kg	SV 20 mg/kg
6th week+	7.02±0.37	6.91±0.19	7.27±0.16	7.04±0.13
7th week	4.58±0.09	4.71±0.05	4.80±0.15	4.58±0.21
8th week	4.25±0.13	3.86±0.12*	3.82±0.04*	3.70±0.10**
9th week	4.14±0.21	3.51±0.06*	3.44±0.02**	3.43±0.06**
10th week	3.89±0.14	3.36±0.05**	3.32±0.02**	3.31±0.04**
11th week	3.71±0.09	3.27±0.04**	3.28±0.02**	3.28±0.04**
12th week	3.61±0.07	3.25±0.03**	3.24±0.02**	3.26±0.03**
13th week	3.56±0.06	3.26±0.03**	3.29±0.02**	3.23±0.03**
14th week	3.59±0.05	3.33±0.03**	3.38±0.02**	3.22±0.03**
15th week	3.66±0.04	3.41±0.03**	3.40±0.02**	3.25±0.04**
16th week	3.74±0.03	3.49±0.03**	3.44±0.02**	3.29±0.04**

<sup>#</sup> Mean values are based upon 6 number of observations

+ Without drug and saline treatment

\* Significant (P < 0.05)

\*\* Highly significant (P < 0.01)

observed that SV enhanced the feed intake in rats. In the present study also an appreciable increase in feed intake (12-22%), body weight gain (19 - 39%) and improvement in feed efficiency (7 - 13%) were observed in a dose dependent manner (Table 4). Body weight of 1.5 kg was reached at the end of fourteenth week itself in all the treatment groups as against the control group in which the same was obtained at the end of sixteenth week only.

The carcass weight (in grams) at the end of the experiment (Table 5) in all the three doses showed highly significant increase (P < 0.01). The increase in dressing

percentage at the end of the experiment was significant (P<0.05) and highly significant (P<0.01) at 15 and 20 mg/kg respectively.

The longissimus muscle area (in cm<sup>2</sup>) showed increase (Table 5) at 20 mg/kg dose alone whereas the other two doses (10 and 15 mg/kg) did not produce any significant alteration. The carcass protein percentage was not altered by SV in all the three doses tested. There was an increase in carcass fat percentage with all the three doses of SV which was significant (P < 0.05) at 10 mg/kg and highly significant (P < 0.01) at both 15 and 20 mg/kg dose levels (Table 5).

Table 4 Effect of sodium valproate on growth in rabbits (Mean  $\pm$  SEM)<sup>1</sup>

Parameters		Growth response with administration of		
		SV. 10 mg/kg	SV. 15 mg/kg	SV. 20 mg/kg
Initial body weight (7th week) (Gm)	Control	412 $\pm$ 3.07	412 $\pm$ 3.07	412 $\pm$ 3.07
	Treated	409 $\pm$ 3.27	409 $\pm$ 3.27	418 $\pm$ 1.05
	Difference	-3	-3	+6
Final body weight (16th week) (Gm)	Control	1519 $\pm$ 9.70	1519 $\pm$ 9.70	1519 $\pm$ 9.70
	Treated	1730 $\pm$ 20.40**	1847 $\pm$ 5.30**	1956 $\pm$ 18.30**
	Difference	+211 (14%)	+328 (22%)	+437 (29%)
Cumulative weight gain (16th week) (Gm)	Control	1107 $\pm$ 6.54	1107 $\pm$ 6.54	1107 $\pm$ 6.54
	Treated	1321 $\pm$ 7.57**	1438 $\pm$ 3.82**	1538 $\pm$ 18.01**
	Difference	+214 (19%)	+331 (30%)	+431 (39%)
Cumulative feed intake (16th week) (Gm)	Control	4131 $\pm$ 22.76	4131 $\pm$ 22.76	4131 $\pm$ 22.76
	Treated	4613 $\pm$ 19.77**	4938 $\pm$ 24.59**	5053 $\pm$ 36.69**
	Difference	+482 (12%)	+807 (20%)	+922 (22%)
Cumulative feed efficiency	Control	3.74 $\pm$ 0.03	3.74 $\pm$ 0.03	3.74 $\pm$ 0.03
	Treated	3.49 $\pm$ 0.03**	3.44 $\pm$ 0.02**	3.20 $\pm$ 0.04**
	Difference	+0.25 (7%)	+0.30 (8%)	+0.49 (13%)

<sup>1</sup> Mean values are based upon 6 number of observations

\*\* Highly significant (P &lt; 0.01)

() Figures in parenthesis are difference between the treated and the control values in percentage

Table 5 Effect of sodium valproate on carcass quality in rabbits (Mean<sup>#</sup>  $\pm$  SEM)

Parameters	Sodium valproate (dose levels)			
	Control	10 mg/kg	15 mg/kg	20 mg/kg
Carcass weight (g)	855 $\pm$ 16.50	994 $\pm$ 3.70**	1008 $\pm$ 4.40**	1208 $\pm$ 4.90**
Dressing percentage	55.16 $\pm$ 0.87	56.96 $\pm$ 0.17	57.90 $\pm$ 0.15	59.74 $\pm$ 0.42**
Longissimus muscle area (cm <sup>2</sup> )	1.23 $\pm$ 0.02	1.22 $\pm$ 0.05	1.37 $\pm$ 0.21	1.40 $\pm$ 0.00**
Carcass protein (9%)	20.07 $\pm$ 0.26	20.46 $\pm$ 0.22	20.37 $\pm$ 0.14	20.74 $\pm$ 0.39
Carcass fat (%)	2.22 $\pm$ 0.06	3.03 $\pm$ 0.26*	3.27 $\pm$ 0.14**	3.14 $\pm$ 0.13**

<sup>#</sup> Mean values are based upon 6 number of observations

\* Significant (P &lt; 0.01)

\*\* Highly significant (P &lt; 0.01)

Table 6 Effect of sodium valproate on serum protein and cholesterol in rabbits (Mean $\pm$ SEM)

Parameters	Sodium valproate (dose levels)			
	Control (Normal saline)	10 mg/kg	15 mg/kg	20 mg/kg
Serum total proteins (g/dl)	7.19 $\pm$ 0.18	7.14 $\pm$ 0.13	6.90 $\pm$ 0.10	7.33 $\pm$ 0.11
Serum albumin (g/dl)	4.79 $\pm$ 0.10	4.93 $\pm$ 0.14	4.37 $\pm$ 0.12	4.79 $\pm$ 0.13
Serum globulin (g/dl)	2.57 $\pm$ 0.26	2.21 $\pm$ 0.10	2.53 $\pm$ 0.19	2.54 $\pm$ 0.12
Serum cholesterol (mg/dl)	88.98 $\pm$ 1.94	80.31 $\pm$ 4.93	91.15 $\pm$ 0.27	99.54 $\pm$ 1.34**

\* Mean values are based upon 6 number of observations

\*\* Highly significant (P < 0.01)

The serum total protein levels (g/dl) were not altered by SV in all the three dose levels tested (Table 6). There was no significant difference between the control and the SV treated groups in serum albumin (g/dl) levels. No significant change in serum globulin (g/dl) levels was observed in any of the SV treated groups. SV at 10 and 15 mg/kg did not cause any significant alteration in the serum cholesterol levels (mg/dl). But there was highly significant (P < 0.01) elevation of serum cholesterol level at 20 mg/kg (Table 6). There was no known reports available regarding the effect of SV in rabbits on serum total proteins, albumin, globulin and serum cholesterol. However, Tanazawa *et al.* (1980) reported hypercholesterolemia in rabbits, induced by dietary manipulation.

## Summary

The effect of oral administration of Sodium valproate - a putative GABA agonist, on growth, carcass quality, serum protein and serum cholesterol in cross-bred male rabbits at the dose levels of 10,15 and 20 mg/kg

daily for ten weeks, from seventh to sixteenth week of age was studied. Sodium valproate significantly increased the feed intake, body weight gain and improved the feed efficiency at all the three dose levels. Carcass weight was significantly increased in all the dose groups but dressing percentage was seen increased at 15 and 20 mg/kg dose only. Longissimus muscle area was seen increased at 20 mg/kg dose only. There was increase in carcass fat percentage at all the dose levels and an increase in serum cholesterol was observed at 20 mg/kg only. Carcass protein percentage, serum total proteins, albumin and globulin were not influenced by any of the doses. Sodium valproate was found more satisfactory in improving growth rate and carcass quality at 10 and 15 mg/kg.

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